

PRIMARY CARCINOMA OF THE PROSTATE.

BY GEORGE W. HAWLEY, M.D.,
OF SEATTLE, WASHINGTON.

No one can scan the literature and fail of the opinion that the popular beliefs in regard to cancer of the prostate are vague and incomprehensive, often misleading, for the most part in error, and in need of elucidation and revision. To quote Eduard Kaufmann,¹⁰ by whom this subject has received exhaustive and careful study: "Die Lehr-und Handbücher bringen über dieses Thema nur wenig, zum Theil auch Falsches." Moreover, it is impossible after a search of the writings to overlook the fact that this disease has enlisted but casual interest and investigation in this country; that during the past decade the work of a few European observers has enriched our knowledge of the pathology necessitating reconstruction of our conception of prostatic cancer.

In few conditions has surgical science been more backward, and few malignant involvements illustrate so beautifully the peculiar features of development—favorite modes of local growth and sites for metastatic deposit—which malignant disease so frequently exhibits in different organs and which require careful notation and consideration if we would hope to recognize prostatic cancer, and apply measures of relief, with intelligence.

It is therefore not unbecoming, especially in view of the evidence that carcinoma of the prostate is more common than formerly believed, and radical cure possible in early cases, to entertain a closer scrutiny and obtain a more comprehensive and definite picture of this oft overlooked disorder.

OCCURRENCE.

In General.—Prostatic cancer has long been catalogued among the rare malignant affections, the basis for such classifi-

cation resting not alone on clinical facts, but in the mass of post-mortem records. Despite such proof, the opinion has been for some time current that this disease is less infrequent than statistics indicate; that it often passes unrecognized *in vivo* and at necropsy. This view has received confirmation in the broadening of our knowledge concerning the morbid anatomy of prostatic cancer. It has been demonstrated that carcinoma of the prostate is often extremely difficult of post-mortem diagnosis without the aid of the microscope. The futility, then, of obtaining an accurate estimate of the frequency of prostatic cancer is apparent, inasmuch as no long series of autopsies is to be found which includes a systematic and careful examination of the prostate. Present post-mortem records are palpably inadequate, for not only do prostates which are macroscopically altered sometimes escape observation, but of those which have received gross examination few have obtained histological diagnosis. Illustrative of the inaccuracy of post-mortem records are the results of Albaran and Hallé's¹ investigation—the finding of several cancerous prostates among those labelled hypertrophy in the Musée Guyon.

While it is quite probably true that the statistics which have been put forward represent but an unknown fragmentary estimate, and it is necessary to bear this in mind, they are worthy of perusal. It is significant that more recent and accurate figures give an increased percentage for prostatic cancer; not that it is believed to be of more frequent occurrence, but that it has less often escaped detection.

Ratio of Prostatic Cancer to Pan-cancer.—The statistics popularly quoted are those of Tanehou published more than half a century ago. In 1844, he collected from the Paris death-register 8289 cases of cancer, finding only five in which the disease was located in the prostate among the 1904 male subjects,—a ratio of 2.6 per 1000. Von Winiwarter, in a *résumé* of the cancer cases occurring in Billroth's clinic during 1868-1875, cites one prostatic in a total of 548 cases of carcinoma (290 men),—a ratio of 3.4 per mille. Heimann, in 20,544 cancer cases recorded in Germany during the two years

1895-96, reports thirty-four as occurring in the prostate (8127 male),—a ratio of 4.18 per mille. The increase shown in the latter figures is pertinent, and gives weight to the declarations of a few investigators who maintain that careful observations will prove many cases diagnosed prostatic hypertrophy to be in reality carcinoma, and cancer a disease of unexpected frequency.

Prostatic Cancer in Urogenital Clinics.—In addition to the above, clinical records have an interesting bearing on the frequency of prostatic cancer. Engelbaeh¹⁰ in 1898 found, during nine months, four cases of carcinoma of the prostate out of 700 patients in Neeker Hospital. Burekhardt⁶ (1902) similarly found fifteen out of 167¹¹ genito-urinary cases during several years. Of this number¹² 86 were prostatic disorders, including inflammations, hypertrophy, etc. Oraison²⁵ (1903) reports twenty-eight of cancer among 306 "prostaties" at Neeker Hospital during the last three years, and at Saint André sixteen out of 170 cases in twelve years. These figures again lend evidence of the relative frequency of prostatic cancer, and with post-mortem statistics go far to corroborate the utterances of those who have given this matter thought as expressed by Labadie,²³ who says, "La cancer de la prostate est une affection relativement fréquente," and Harrison¹⁷ who remarks, "My belief is that carcinoma of the prostate is far more common than we have been led to think."

*Sarcoma * and Carcinoma.*—Formerly very little, if any, distinction was made between sarcoma and carcinoma. Bellfield² states that seven-eighths of prostatic tumors are found to be carcinoma, the remainder sarcoma. Von Frisch¹² gives 85-90 per cent. as the frequency of cancer in malignant disease of the prostate. Unanimous are all writers that carcinoma is much the commoner.

* Consideration of sarcoma is purposely omitted in this paper because confusion is to be avoided, and—more important—because sarcoma, unlike carcinoma, does not offer the same difficulties of diagnosis, rarely simulating or occurring at the same age as hypertrophy. Sarcoma is propense to more extensive and diffuse growth. As a rule, it occurs before thirty, often in childhood, very occasionally after fifty.

Primary and Secondary Involvement.—As a rule, malignant disease of the prostate is primary. Secondary involvements, as Kaufmann has pointedly declared, are rare, and then usually due to direct extension from neighboring organs. Of sixty-two cases of malignant disease of the prostate, Engelbach found only eleven (17 per cent.) to be of secondary origin. To these Burekhardt added two more and sought the primary focus. Seven of the thirteen proved to be the result of direct local extension from the rectum, bladder, and penis. The remainder represented metastatic deposit from remote organs, such as the stomach, lungs, dura mater, etc.

Cancer in the Hypertrophied Prostate.—While this condition has been questioned, doubt no longer can exist that cancer does develop in so-called simple enlargement, and it is presumable that these cases of *hypertrophy-cancer* are not infrequent. Cases of this kind were reported by the older writers, notably, Sir Henry Thompson,²⁰ Klebs, and Socin. Richard Wolff²¹ mentions nine such cases, and Burekhardt relates a case of carcinoma which unquestionably developed in an hypertrophied prostate. Greene and Brooks¹⁴ record three cancerous out of fifty-eight hypertrophied organs examined. Albaran and Hallé, who have given particular study to this question, found evidences of cancer in fourteen out of 100 enlarged prostates, and Belfield,³ in his remarks upon their work, opines "That their contention is amply supported by general clinical experience." Greene,¹⁵ in a paper presented at the last meeting of the American Association of Genito-urinary Surgeons, places the frequency of these hypertrophy-cancer cases at from 5-10 per cent., a conservative estimate as judged from the above figures.

Carcinoma in the Atrophic Prostate.—The similarity in the nature of the two processes—hypertrophy and atrophy of the prostate—has been emphasized by Ciechanowski⁷ and Crandon,⁹ and von Recklinghausen²⁰ has called attention to cancer in the atrophic as well as in the hypertrophied gland. In one of his cases the prostate was atrophied, measuring only thirty-five by twenty millimetres. Additional cases have been

observed by von Frisch, Julien,¹⁸ and others. While atrophy itself is uncommon and *atrophy-cancer* must be still rarer, it is a point of clinical moment to know that this dual condition may exist.

ETIOLOGY.

The pathogenesis of carcinoma of the prostate is a subject at once a part of that branch of pathology which concerns malignant disease in general and beyond the compass of this article. Suffice it to say that of the various hypotheses which have been advanced,—bacterial, parasitic, cell-reversion, etc.,—the so-called chemical theory claims particular attention in prostatic disease. A thesis ascribing carcinoma, and likewise hypertrophy, to chemical or physical action of pathologic substances derived from the prostatic secretion is a plausible one. In few glands are the conditions more favorable for the development of morbid bodies or of normal ones in pathologic quantity. The prostatic secretion is not only of a highly complex nature, but subject normally to extraordinary variations. It is quite rational to suppose that very little would be required to produce such pathologic substances; that diminished nutrition and non-activity as seen in the old may be sufficient factors, as well as chronic inflammation following gonorrhœa. In evidence of formation of morbid chemical bodies in the prostatic secretion may be mentioned the corpora amylacea.

While it is not to be supposed that hypertrophy or cancer results from every heteroplasmic substance developed in a perverted prostatic secretion, it is reasonable to believe that there may be formed certain bodies which have such action. At any rate the chemical thesis—in the case of the prostate—appears endowed with as much logic as any now in favor, and subserves the tenet, projected by Ciechanowski, that a chronic inflammatory process in the prostate is indispensable to senile changes.

It is interesting to note that von Hoffmann, who has chemically examined the hypertrophied prostate, observed the presence of certain substances not found in the normal gland. Similar investigations as to the character of the prostatic secretion in cancer and in hypertrophy may throw some light on this subject.

Predisposing Causes.—The gonococcus infection of the urethral tract has been extensively argued as an etiological factor both in hypertrophy and in cancer. Its relation to these two morbid changes has not been definitely made out. The probabilities are that gonorrhœal infections of the intrapelvic urethra and prostate are factors in the production of prostatic hyperplasia and cancer. On the other hand, these diseases unquestionably develop independently of, and years after, a gonorrhœa. And of all the "gonorrhœics" but a moderate proportion become afflicted with these senile sequelæ. The evidence compels the placing of urethritis among the predisposing causes, as Ciechanowski has done, when in discussing the etiology of hypertrophy and emphasizing chronic inflammation as an essential forerunner, he conservatively adds that the inflammatory process may be due to, although it does occur without, a gonorrhœa.

Julien sought the frequency of urethritis in forty-seven cases of prostatic carcinoma, finding it positive in twenty-one, negative in nine, and questionable in seventeen. Burchhardt, in ten personal cases, reports only one in which there had been a previous urethritis.

Age is a notable feature. Cancer of the prostate has rarely been met with before fifty. In this respect it resembles hypertrophy and contrasts with sarcoma. Of 100 cases collected by Kaufmann all were over forty, only eight under fifty, and 68 per cent. between fifty and seventy. A few cases have been observed under forty. Wolff found six cases in the literature, the youngest being twenty-nine. Heredity, climatic, racial, and other conditions, as predisposing causes, are unimportant, and bear the same relations to prostatic as to cancer of other organs.

PATHOLOGICAL ANATOMY.

It is only within the last decade or so that the morbid anatomy of prostatic cancer has received anything approaching satisfactory investigation. Previous to this the knowledge of the pathology was crude and restricted. Sarcoma and carcinoma were confused; so much so that from the older records

it has been impossible to separate the one from the other, although it is known now that cancer never occurs in infancy, notwithstanding a few cases so diagnosed formerly. For many years only one form of carcinoma was recognized, namely, the massive, rapid growth later aptly called by Felix Guyon "carcinoë prostato-pelvienne diffuse." Occasionally other forms were described to which the terms "fringoid," "encephaloid," and "scirrhous" were attached. Thompson was probably the first to call attention to the small, hard, scirrhous cancer. Later, Fenwick¹¹ announced his belief in the predominance of this form, which he likened to mammary scirrhus. This it closely resembles, but von Frisch has pointed out that the term is, histologically speaking, incorrect. Concerning extension and metastases nothing definite was known.

Upon such meagre knowledge of the pathology, the descriptions of prostatic carcinoma have been necessarily vague and often contradictory. This largely holds true to-day. By many we are told that this disease is characterized by extensive growth, by others that in the majority of cases it is of the small scirrhous type. Of metastases, we read that glandular involvement is quite invariable, with rare but brief reference to invasion of the bones.

With the splendid work of von Recklinghausen (contributed to the *Festschrift* in honor of Rudolph Virchow in 1891), who first brought out the richness and frequency of skeletal metastases, together with the more recent extensive investigations of Kaufmann, who has not only studied critically his own many cases, but all authentic records in literature, has the pathological anatomy been placed on a broad and comprehensive basis. The result of their work has been to show that, grossly, several forms of prostatic cancer are to be recognized; that the so-called common massive type is in reality rare; that histologically several distinct and mixed varieties are found which develop in the hypertrophied, normal, and atrophic gland; that carcinoma tends not to regional extension nor to ulceration; that metastasis to the lymph-glands is not as common as in carcinoma elsewhere, but, on the other hand, is

exceedingly frequent to the bones and quite general throughout the skeleton. These two investigators have also emphasized the difficulty of post-mortem diagnosis by naked-eye appearance alone. Even the sight of the skilled pathologist often fails to detect carcinoma in the prostate. To distinguish between hypertrophy and hypertrophy-cancer is particularly difficult. Microscopical diagnosis is essential in the majority of cases, as Kaufmann²⁰ has foreihly declared. Interesting in this regard is the case of Sasse,²⁸ in which diagnosis failed during life. Autopsy revealed an enlarged prostate and rich carcinomatous metastasis in the bones. On careful gross examination it could not be said whether the prostate was cancerous or not. The microscope disclosed cancer.

GROSS ANATOMY.

Size and Form.—Four forms of prostatic cancer have been distinguished: (1) The *very small*, which includes only those cases of atrophy-cancer with limited growth. (2) The *small*, in which the prostate is of about normal size. (3) The *large*, in which the prostate is enlarged by reason of carcinomatous growth or from the condition of hypertrophy-cancer. (4) The *very large* or the enormous pelvic form. All are found at autopsy, which fact confirms the belief that the primary growth may be very small, even in the late stages. The first three forms collectively, in comparison to the massive type, occur in the proportion of about seven to one.

Thus, Kaufmann out of 100 cases found only fourteen of Guyon's carcinose diffuse. These findings are consonant with Harrison's statement that "carcinoma of the prostate, in by far the larger proportion of cases, is small and of slow-growing nature."

Location and Local Growth.—With few exceptions the disease process is situated in the recto-urethral prostate, in one or both of the lateral lobes, or more rarely in the middle lobe. Only very infrequently has the pre-urethral portion of the prostate been found invaded. Carcinoma begins usually as one or several small nodules, which may remain quite stationary

throughout the course of the disease, yet giving rise to extensive and virulent metastases. The process may involve only a portion of the whole of one or both lateral lobes, more rarely the whole gland. Emil Burckhardt recounts an unusual case in which the disease was limited to the middle lobe, causing an elevation of the bladder floor.

Surface changes are usually noticed. An irregular, nodose appearance of the external surfaces and borders of the portion of the gland involved is the rule. Mechanical displacement of adjacent structure due to expansion of the prostate is not great except in hypertrophy-cancer, largely owing, perhaps, to the fact that the middle lobe is rarely involved.

Consistency.—Cancer of the prostate is characterized by distinct hardness, often spoken of as a "stony-hardness." It is this feature which gave rise to the term *scirrhus*. So prominent is this phenomenon that Guépin¹⁰ looks upon it as a clinical sign of almost pathognomonic value, and lays great stress upon it in the differential diagnosis. Very occasionally softness has been described which has invariably proved to be central caseous areas in large nodules. Cases in which soft areas were noted have been reported by Wyss, Wolff, and von Recklinghausen.

Cut Surface.—To the practised eye are revealed spherical nodes—when these are of more than microscopic size,—varying from a granule to a filbert—exceptionally found as large as a goose-egg. Distinguishing features are often lacking. Sometimes of a reddish-gray color, these nodes contrast strangely with the prostatic tissue. The so-called cancer juice may at times be clearly demonstrated, but is frequently lost in the secretion of the gland.

Degenerative Changes.—Although breaking down and ulceration occur in the later stages, carcinoma of the prostate does not tend to such changes, which are invariably the result of extension. When ulceration does take place it is usually towards one of the adjacent mucous membranes,—oftenest the urethra, then the bladder, less so the rectum. In the diffuse pelvic form, pronounced destruction may be found giving rise

to recto-urethral fistulae, peritonitis, phlegmon, etc. Catheterization and instrumentation are held to play an important rôle in the production of degeneration.

Regional Invasion.—While many of the older writers contended that a tendency to infiltration was characteristic of prostatic cancer, the opposite view is prominent of late. Englehardt maintains that local extension is not the rule, and Kaufmann, from an analysis of 100 cases, places its occurrence at about 57 per cent. Local metastatic dissemination appears in the form of small nodules beneath the mucosa of the urethra and vesical trigone and mouths of the ureters, into the seminal vesicles, less frequently into the rectum and pelvis. These processes rarely proceed beyond fixation of the mucous membrane. In only five cases did Kaufmann find vesical ulceration. Instances of metastases in the posterior portions of the corpora cavernosa of the penis have been reported.

HISTOLOGICAL ANATOMY.

Several varieties of carcinomata have been described, but it is sufficient here to briefly remark on the three usually met with. The least common of these is, perhaps, the *adenocarcinoma*, then the *medullary* or *carcinoma solidum*, and (most frequent) the combined form. A true scirrhous cancer has very exceptionally been observed, and another rare species is that which Ciechanowski has styled, "Adenoma destructens malignum."

Adenocarcinoma resembles very closely the non-malignant adenomatous growth found in the so-called hypertrophy. In both there is builded glandular tissue lacking characteristic features. The alveoli in both may be distended with desquamated epithelial elements with central detritus-bearing areas. In carcinoma, however, there exists usually less space between the alveoli, the cell-nuclei stain deeper, and the lymph-spaces often contain cancer-cells.

Carcinoma solidum is characterized by the presence of areas of small round or cubical cells with large, deeply-staining nuclei. Large and small groups are found, and scattered cells

are often seen between the connective-tissue fibres and in the lymph-spaces.

In the mixed variety the characteristics of medullary and adenocarcinoma appear in varying proportion. But while a pure medullary carcinoma is frequently seen, an adenocarcinoma without some traces of the former is rare.

In all varieties may be found areas of round-cell infiltration, as in hypertrophy; also nests of cancer-cells invading the lymph-spaces, the sheaths of the nerves, and the blood-vessels, particularly the veins. These are often found completely filled, their walls having been penetrated.

METASTASES.

Unquestionably the most striking feature in the complex picture presented by primary cancerous disease of the prostate is found in its secondary metastases, which are at once peculiar, frequent, and profuse. Peculiar, because, as a rule, specific sites are chosen for metastatic invasion. Frequent, because it occurs in more than a majority of cases, and profuse, since secondary deposit is invariably far in excess and out of proportion to the primary growth. While the latter is usually small, the metastases from it are usually excessive.

The favorite metastatic sites are the bony skeleton and lymphatic glands.

Glandular involvement has been considered almost an in-failing sequence. Conc,⁸ on the other hand, from a study of the literature and of his own case reported from Halsted's clinic, concludes that the lymph-glands may not be involved. He found glands which were enlarged, but only one containing cancer elements. Kaufmann, who has more recently elaborated upon glandular metastasis, remarks on its infrequency when compared to carcinoma of other structures. In his twenty-two personal cases, it was met with in eleven (50 per cent.).

The glands usually invaded are the pelvic, the iliac, and the inguinal; also the mesenteric, hepatic, mediastinal, supra-clavicular, and axillary. In Kaufmann's 100 collected cases, the pelvic glands were involved in twenty-seven, the iliac in

twenty-four, and the inguinal in sixteen. Metastasis takes place through the lymphatic channels, and into the inguinal chain, probably secondarily from the pelvic glands or rarely from the corpora cavernosa, and not directly from the prostate.

Deposit in the Bones.—It is generally conceded that carcinoma of bone is never primary, always secondary. The three chief sources of osseous cancer are primary disease of the breast, of the thyroid, and of the prostate. Of these, prostatic carcinoma is most prone to this remote extension.

Thompson was the first to record such a case in which numerous carcinomatous foci were found in the vertebræ. Little, however, was known or thought of this complication until von Recklinghausen in 1891 called attention to its frequency, and graphically described the morbid anatomy. Following the publication of his five cases many others have been reported, including the interesting one by Cone in this country. But the number of reported cases in nowise furnishes an idea of its frequency, because so seldom are the bones carefully examined at necropsy; the more true since usually they manifest but little or no external evidence of disease. Von Recklinghausen, in commenting on one of his cases, says that the bones would not have been examined had not one prominent surface bone (the frontal) presented a small tumor.

Conclusions drawn from an inspection of the bulk of cases in literature necessarily represent a low estimate. The earliest statistics are those of Wolff (1899), who found record of bone metastasis in nine of eighty-three prostatic cancers, 13 per cent. Kaufmann's figures (1902) are somewhat higher, 34 per cent. in 100 cases. An accurate conception is only possible from a comprehensive calendar of cases, in each of which careful post-mortem sections, including skeletal examination, have been made.

The only list of such character at present obtainable is that by Kaufmann. In his twenty-two cases, secondary skeletal involvement was found in sixteen, 72 per cent. Whether such a high ratio actually prevails awaits confirmation. At any rate,

these figures indicate, as their compiler observes, a frequency far in excess of all imperfect notions previously held.

Metastasis in the bones is, as a rule, more or less general. Rarely are only one or two bones affected. In this respect Cone's ease is typical, with disease of three lumbar vertebrae, one rib, ilium, and tibia. In only one instance among Kaufmann's sixteen cases was but a single bone diseased. A predilection is observed for certain bones. The vertebrae hold first place as a favorite site (particularly the lumbar), then the ilium, femur, ribs, humerus, sternum, calvarium, tibia, etc. Of the thirty-four cases of skeletal metastases collected by Kaufmann, the lumbar vertebrae were involved in twenty-seven, the ilium in twenty-one, the femur in twenty-three, ribs in nineteen, sternum in twelve, skull in twelve, tibia in six.

Space forbids more than a brief consideration of the anatomic changes, for the details of which reference may be had to the excellent description given by Dr. Sidney M. Cone (*Bulletin of the Johns Hopkins Hospital*, May, 1898, p. 114). Von Reeklinghausen's belief, that the bone marrow is primarily the seat of deposit, is generally accepted as the true one. The soft parts of the bones are usually found invaded by small nodules of cancer-tissue histologically resembling the type of the mother-growth in the prostate. In the long bones these occur more frequently near the epiphyses,—in the vertebrae throughout the spongy portion of their bodies. This "osteoporosis," "myelogenous carcinomatosis," or "osteoklastic" process, often extends from the central canal to the periosteum, through the cancellous structure *via* the Haversian system, in which may be found nests of cancer-cells. Extension to the periosteum is productive of an "osteosclerosis," "fibroperiostitis," or "osteoplastic" process with the formation of new bone.

This osteoplastic process occurs most frequently in the flat and long bones, giving rise to irregularities and small tumefactions of their surface. Rarely, however, do more than one or two bones show such changes. New bone formation also occurs in the marrow.

These two processes—osteoklastic (called by von Reek-

linghansen "osteomalacia carcinose") and osteoplastic—are rarely productive of any great destruction of the bones, on the one hand, or of malformations or tumors of any size, on the other. The two largest tumors on record appear in Cone's case and in one by Kaufmann (see appendix). Spontaneous fractures have occurred in but one or two instances.

Von Eiselsberg's view as to the mode of transmission in carcinoma of the thyroid has been accepted in prostatic cancer. The veins are considered the source of dissemination. This thesis possesses probability, since phleboliths are common in the prostatic veins. But why the cancer elements (since they must pass to the right heart, through the pulmonary circulation and into the general arterial stream) should be deposited with such regularity in the bones instead of in the lungs or other organs is still obscure. Explanatory hypotheses include a chemical affinity on the part of the bone marrow, a mechanical entrapment, and Neusser adds a most ingenious theory based on the assumption of a "blood-relationship" between the mammae, the thyroid, the prostate, and the bone marrow.

The marked similarity of secondary carcinoma of the bones from prostatic, thyroid, and mammary cancer is an interesting pathological coincidence which has baffled explanation. Carcinoma of the breast and of the thyroid choose with almost equal regularity the same bones as the prostate. In four cases of breast cancer with skeletal carcinomatosis, seen post-mortem by the writer, the vertebrae, ribs, femora, etc., were invaded, but in none was there any external evidence of disease. According to Limacher, this complication occurs in 37 per cent. of cases of cancer of the thyroid. The rate in mammary disease is given by Lenzinger as 14 per cent. Skeletal cancer occasionally occurs in cancer of the uterus and of the stomach.

Internal metastasis is found with some degree of frequency. Specific selection of any organ or group of organs is lacking. Kaufmann places the occurrence of internal metastasis in about 25 per cent. of cases. He found metastases in the liver, lungs, peritoneum, dura mater, pancreas, adrenals, spleen, thyroid,

endocardium, etc. These involvements are believed to be retrograde from the lymph-glands.

SYMPTOMATOLOGY.

The symptoms of carcinoma of the prostate, for the sake of clearness, may be classified as follows: (1) Those due to the primary disease in the prostate; (2) those arising from local invasion or displacement of neighboring organs (principally urethra and bladder); (3) those produced by secondary disease of the bones, lymph-glands, and internal organs. It is significant that those belonging to the first group are sometimes absent or indistinctive, and invariably attributed to other causes, which is perhaps even truer of the metastatic phenomena for the reason that they are more or less identical with those of more common disorders, which often coexist, masking the more serious malady. While, generally speaking, the symptoms of prostatic cancer are lacking in distinguishing characteristics, one or two observers have pointed out that certain features are usually present which are of particular diagnostic value.

To avoid repetition, the signs and symptoms will be discussed as usually given and not as classified above.

Pain.—Of first importance is that due to the primary growth in the prostate. This is more often vague and irregular, though in some cases dull and persistent. It may be referred to the perineum, rectum, glans penis, and often radiating to the hypogastrium, back, and thighs. Rarely severe, it may disappear for periods or altogether.

Secondary pain occurs as the result of glandular enlargement and disease of the bones. The former usually manifests itself as a sciatica, usually bilateral. Skeletal pain simulates the so-called chronic "rheumatic" pains of the old, for which it is usually mistaken.

While Belfield⁴ and others are impressed with the frequent painlessness of prostatic cancer, there are some observers who state that there are few cases which are entirely free of pain at one time or another,—few in which pain, though vague,

is absent in the early stages. Pain in the region of the prostate is certainly an important symptom, because usually the one guide leading to early diagnosis. Persistent pain in or about the prostate in elderly men, developing in the course of hypertrophy, should awaken a lively suspicion and call for careful investigation. The importance of this symptom is beautifully illustrated in Greene's case (see appendix), in which "operative procedures (prostatectomy) for the relief of pain became imperative," and removed what turned out to be an early carcinoma of the prostate.

The pain of cancer is to be differentiated from that of vesical calculus and tumor, prostatic stone and tuberculosis, of rectal cancer, of pelvic neuralgia, and prostatic neurosis.

Urinary phenomena are dependent upon elevation of the vesical outlet, or cancerous invasion of the urethra and bladder, or both. The former is rarely sufficient to produce symptoms except when combined with hypertrophy. Then micturial frequency, residual urine, and pyuria are usually present. Occasionally the displacement due to cancerous enlargement gives rise to some frequency and a small amount of residual urine. Vesical and urethral invasion only add symptoms when such results in ulceration with haematuria.

According to von Frisch, the urine in neoplasms of the prostate usually remains normal for a long time. Fenwick accords urinary symptoms in about 60 per cent. of all cases. In the case of Sasse (*vide supra*) the urine was notably clear (normal).

Haematuria is given as occurring in 26 per cent. of cases by Engelbach, in 37 per cent. by Burckhardt. The blood either appears more particularly at the beginning, or at the end, of the stream, or thoroughly mixed in the urine. The haemorrhage is usually continuous, though at times may subside. Occasionally it is profuse.

Retention of urine is rare, generally seen in large hypertrophy-cancer or diffuse cancer.

Rectal symptoms are infrequent. Constipation is met with in large growths, and haemorrhage very rarely from ulceration.

Rectal Examination.—Characteristic of carcinoma prostate to the exploring finger are hardness, tenderness, and a rough, nodular contour of the rectal surface and margins of the lateral lobes. Sometimes a single hard spot, a projecting node, or a lobulated surface or border of one or both lobes are distinguished. Irregular enlargement of one or both lobes is the rule. In hypertrophy-cancer, smooth, bulging expansion, in which more or less distinct dense, sometimes protruding, areas are found. Tenderness is rarely great, and is usually localized in the portion of the gland diseased. While these signs are sometimes with difficulty made out, von Frisch, Guépin, and others evince the belief that they are usually present, and when prominent are diagnostic.

Signs of extension into the rectum are found in fixation of the mucous membrane to the prostate, and in small shot-like nodes adherent to the mucous surface. Extension into the seminal vesicles can sometimes be demonstrated by their indurated, enlarged, lobulated feel. Diseased pelvic glands have been palpated (with the lower bowel empty) by sweeping the finger high up along the sides and sacral region of the pelvis. In diffuse pelvic carcinomatosis, indurated areas may be made out, extending outward from the prostate, which is more or less immovable, and when extensive, as Keyes²¹ remarks, "the finger abuts upon an enormous hard, nodular tumor."

Cystoscopic and Urethroscopic Examination.—The cystoscope may reveal alterations in the contour of the vesical outlet and trigone, due to expansion of the prostate, and a nodular appearance of the infiltrated mucosa or ulceration may be seen. These signs are negative unless taken in conjunction with the symptom complex. The most positive one is, perhaps, the picture displaying a tubercled appearance of the mucous membrane of the vesical floor and ureteral openings. Even then correct interpretation is often difficult.

Endoscopic pictures of the intrapelvic urethra may evidence ulceration, deep excavation, papillomatous formation, or a normal mucous membrane. According to von Frisch¹³ such findings in themselves are of little diagnostic value. The

urethroscope is perhaps of value in determining the question of urethral involvement.

Cachexia is an uncertain symptom except in the very late stage of the disease. It is usually more prominent when metastasis is extensive and quite out of proportion to the size of the primary growth. Occurring in old men and in old "prostatics," it is often masked by the emaciated senile skin, and mistaken for the septic appearance due to prolonged urinary infection.

The glands, other than those deeply seated, are occasionally enlarged. Most commonly seen are those of the inguinal region. Usually bilateral, they indicate metastasis from the pelvic glands. Supraclavicular and axillary enlargements have been noted. Carlier reports a conspicuous case of the former, adding that supraclavicular gland tumor, especially of the left side, in doubtful cases of prostatic enlargement, points to a diagnosis of prostatic carcinoma.

The Bones.—Secondary tumors are rare, clinically, because so seldom of more than moderate size; they are usually undemonstrable unless very superficially situated. Only a few cases are on record. Von Recklinghausen reports one of the frontal bone; Cone, one of the tibia; and Kaufmann, one of the ilium. It is instructive that the two former were diagnosed osteosarcoma and operated.

Examination of the bones, particularly the ribs, may reveal spindle-shaped, tender swellings. Tenderness over the bones, especially the spines of the vertebrae, is given as an important symptom. Radiographs are of questionable value, although the scant clinical data does not permit decision on this point. Kaufmann in several cases reports negative results.

The Blood.—In carcinoma of the bones, particularly when the bone marrow is infiltratingly diseased, and many and large bones are affected, it would be natural to expect to find alterations in the blood-findings, notably in the elements of supposed myelogenous origin. Such is unquestionably the case in many instances. Braun⁵ gives a case in which poikilocytosis was marked and myelocytes (largely eosinophilic) and normoblasts

were present. Türk, in Neusser's clinic, diagnosed a case * of skeletal carcinosis in breast cancer from the finding of considerable numbers of nucleated red blood-corpuseles and myelocytes in the blood. The autopsy (seen by the writer) was confirmatory. The majority of the vertebrae, as well as several other bones, were diseased. The haematology of carcinomatosis of the bones has been recently studied at some length by Kurpuweit,²² who believes that blood changes are early and constant features, so much so that diagnosis may be made without the supplemental evidence of a primary tumor. According to his observations, the appearance of considerable numbers of myelocytes is characteristic, and upon this is based the diagnosis. He recites thirteen cases upon which his assertions are founded, including earlier cases by Braun, Ehrlich, and Epstein.

Bence-Jones albumosuria has been mentioned as a symptom of myelogenous carcinosis, but some doubt seems to exist in this regard. While a few vague statements to the contrary are to be found, Dr. Parkes Weber,³⁰ of London, who has carefully reviewed all the authentic cases of Bence-Jones albumosuria in literature, is emphatic in declaring that "Metastatic tumors affecting the skeleton, however extensively the bone marrow may be infiltrated, have never yet been known to cause Bence-Jones albumosuria."

Paraplegia has occurred in patients afflicted with prostatic carcinoma with sufficient frequency to demand notice. Thompson observed a case which was due to a small tumor of a vertebrae pressing on the cord. Nélaton records a similar case. Another interesting case by Burekhardt (see appendix) revealed a metastatic mass in the spinal dura, the size of a cherry. Belfield mentions a recent fatal case without autopsy.

Diagnosis.—Wolff has pointed out the difficulty of diagnosis, and von Friseh has given practical expression of it when, in reporting his twelve cases of malignant disease of the prostate in his clinic during ten years, he says that the majority

* Billings and Capps (*The American Journal of the Medical Sciences*, September, 1903) mention this case, and discuss osseous carcinoma in the differential diagnosis of myelogenous leukaemia.

were diagnosed either at operation or at necropsy. The fact is, that the recognition of prostatic cancer depends upon phenomena which may often escape observation and readily avail of misinterpretation. It is particularly unfortunate, since the prostate and its neighboring structures are subject to frequent affections possessing great similarity and often concurrent. Of this hypertrophy is a prominent example. But more significant is the fact that the physical signs depart so widely from those popularly held as characteristic and only too often made the chief diagnostic features of cancer and malignant disease in general, namely, the positive, though varying, increase in size of the primary neoplasm, its inevitable octopus-like grasp upon the surrounding parts, and its final destructive ulceration. Little wonder is it then that this disease in the past has so frequently evaded detection during life. Yet upon a better understanding of the morbid anatomy and symptomatology, and with more acute and intelligent clinical observation, it would appear as though cancer of the prostate should be recognized with greater certainty, and frequently before the stage of metastasis.

While the attention is often called to cancerous disease of the prostate by the symptoms of its metastases, the diagnosis assuredly depends upon prostatic symptoms; not so difficult in the small minority of cases in which growth is progressive and tumefaction grossly obvious; often tentative in the larger number of cases in which the prostate is moderately altered; and often impossible—it would seem—in those few in which the external configuration of the gland is unchanged.

Upon the data at present obtaining, early recognition is dependent upon three not wholly satisfactory phenomena, and these three alone, to wit: Pain in or about the prostate; areas of hardness and nodosity palpable from the rectum; and tenderness. Whether all of these, or the second and most valued one alone, suffice must await future proof. In this connection Greene's case is instructive, for, with a suspected stone or cyst of the prostate associated with pain, a cancerous prostate was removed undoubtedly early and apparently before metastasis.

The diagnosis does not rest with the suspicion or demonstration of prostatic cancer. In view of the prognosis and of possible operative interference, the diagnosis of metastasis, so far as is possible, is paramount. The urine and urinary tract require investigation. Clear urine does not mean vesicourethral freedom from invasion. Haematuria signifies urethral or vesical ulceration, more often the former. Rectal examination is necessary to determine, if possible, whether the rectal mucous membrane is adherent to the prostate; pelvic glandular enlargement; and suspicious induration from the prostate laterally and towards the seminal vesicles. Observations should also include the skeleton, the blood, and the superficial lymph-glands, more especially the inguinal, supraclavicular, and axillary.

Differential Diagnosis.—Carcinoma of the prostate is to be distinguished from hypertrophy, stone, cyst, tuberculosis, neuralgia, and abscess of the prostate; from vesical neoplasms and cancer of the rectum. Hypertrophy has been most frequently mistaken for cancer, because both occur at the same age, because both are characterized by moderate enlargement of the prostate,—often coexistent,—and because of the tendency to call all enlargements in mature men hypertrophy.

The following case is of interest from a diagnostic standpoint, although only probable because uncorroborated by autopsy. This patient I only saw once just before his removal to a distant town, where he soon afterwards died.

J. E. A., sixty-nine years, American, single. Aside from urethritis at twenty had always enjoyed splendid health and strength, having led an active life in many parts of the world. Disease during childhood unrecorded. Luetic infection denied. During the past one and one-half years has suffered pain referred to the rectum, sacrum, and hips. More recently pain in the back, shoulders, and back of neck. These pains have never been severe, though more or less constant. Upon medical advice has conscientiously followed treatment for rheumatism. During past few months has lost considerably in weight. Interrogation elicited nothing further than a long-standing chronic cough, until one

week ago when he "took a cold which settled in the chest," for which consultation is sought.

Status Præsens.—Man of large frame and advanced age, in bed, though able to sit up and move about. Emaciation marked and skin of eacetic appearance. Pulmonary signs of emphysema and subacute bronchitis. No evidence of pneumonic consolidation, fluid or tuberculous process. Temperature, 99° F.; pulse, 78; respiration, 22. Mucous membranes pale. Heart sounds weak. Arteries thickened. Examination of abdomen and extremities negative. Urine clear, examination negative. Rectal examination: Prostate asymmetrically enlarged; left lobe of normal size, shape, and feel; right lobe irregularly enlarged, lateral margin lobulated, and rectal surface corrugated, with prominent nodule of the size of a hickory nut and of extreme hardness. Rectal mucous membrane non-adherent. Entire right lobe moderately sensitive to pressure. Further rectal examination negative (no glandular enlargements or areas of induration felt). Examination of superficial glands negative. Palpation of back for source of pain brought out marked tenderness to pressure upon the spines of the vertebræ, particularly the cervical and lower dorsal. Flat, ovoid, hard swelling felt over the outer surface of the right ilium just below the crest. Further careful examination of skeleton negative, except for slight tenderness over sternum. Catheterism and urethral instrumentation not attempted.

Blood examination: Hæmoglobin, 60 per cent. Estimation of erythrocytes and leucocytes not made. Nucleated red blood-corpuscules (normoblasts) averaging two to the field. Myelocytes in the proportion of one to every three leucocytes to the field. No poikilocytes.

Prognosis.—Carcinoma of the prostate has been classed among the highly malignant and rapidly fatal neoplasms, the duration varying from six months to two years, rarely longer. Its malignancy is displayed, however, rather through extensive metastatic colonies than in the small primary focus.

It is reasonable to suppose that the primary growth itself is, as a rule, a slow process, which would be years reaching a sufficient local growth to cause death were it not that metastases

in the bones, lymph-nodes, and internal organs invariably supervene. The advent of secondary involvement, in amount often many times that of the parent growth, naturally shortens the course of any growth, no matter what may be the degree of its malignancy.

Based upon the morbid anatomy, the operative prognosis is governed not only relatively by the extent of regional growth, but absolutely by secondary remote involvement. Theoretically, removal of the prostate in early cases should result in radical cure by reason of its tendency to remain sessile and embedded within the gland. While the operative experience of forty years, beginning with Billroth in 1859, has been a record of failure so uniform that a stigma has been placed upon surgical intervention amounting to a general, often bitter, condemnation, it has only proven what pathology is ever teaching, namely, that excision of mature malignant tumors can rarely, if ever, be complete. It is noteworthy that in the cases reported during this period no mention is made of early diagnosis. Maturity and metastases were undoubtedly the rule, usually known or suspected by the operator, and evidenced by the symptoms described. As in the early case of Billroth, disease of the bladder or other structures were frequently demonstrated during the operation.

However, to-day a new aspect has been given this subject and a brighter outlook is promised, not alone from pathological study of prostatic cancer, but in recent statistics of operation. That early operation should be curative is given confirmation in Oraison's report of twenty-three cases from the French clinics in which perineal prostatectomy was done. In ten of these (43 per cent.) cure has remained permanent after more than four years; in three only was there recurrence. Six others recovered, but were lost sight of; the remaining four died from the operation.

These figures are certainly most encouraging, and compare favorably with those of cancer of other organs, though hardly surprising, in lieu of the anatomic fitness of uncomplicated prostatic cancer for complete removal. The fact that this

applies only to early disease must not be lost sight of. In late carcinoma of the prostate, as in few other forms of malignant disease, is the prognosis graver. It is upon such cases that the bane of surgical interference must fall. A regret it is, that many of the cases are not seen, or are not recognized until metastases have set in.

Treatment.—Until the cancer problem has been solved, the treatment of malignant disease wherever encountered must of necessity be empirical. The exigencies of the times include radical operative measures, palliative operations, Röntgen therapy, and symptomatic treatment.

The application of radical surgery, at least its scope as a curative measure, must be governed by anatomy of the part and the habit and peculiar features of cancer in local and remote development. Thus in carcinoma of the breast, where lymphatics are numerous and the pathways of early extension to the axilla, to the neck, through the chest wall to the pleura and mediastinum, extensive and early operation is demanded, for success is dependent on removal of lymphatic channels before the penetration through the chest wall and to the deep cervical glands. In like case is carcinoma cervicis uteri, but not so prostatic cancer. Firstly, is the prostate poor in lymphatics; secondly, is cancer not given to diffuse lymphatic dissemination; and thirdly, is the anatomy such that removal of the prostate with surrounding structures becomes impossible. On the other hand, as detailed above, carcinoma prostatæ tend to confined local development, but to diffuse distant metastases. Were the regional conditions the same as in mammary disease, then would prostatic cancer be inoperable in any stage. The redeeming feature lies in the fact that, in a region where operative measures are limited, the extent of the primary tumor is also limited. In carcinoma of the prostate, the requirements of surgical intervention are early, but limited removal of the parts and success are subject to its accomplishments before extraprostatic invasion has taken place.

Radical Operation.—The general prejudicial teachings and the statements that prostatectomy for cancer is "little short

of a calamity" and "absolutely contraindicated"—while based on results, and conserving against the misusage of surgery—are backward leanings and not borne out by pathologic study or recent surgical experience. And yet it would be vicious and disastrous to revert to the other extreme, for there are many cases in which it would indeed be a calamity (except as a judicious palliative measure) to apply surgical intervention. Anatomically, the line of distinction between clearly operable and grossly inoperable is most finely drawn. Furthermore, as in few diseases, are we so reliant upon the presence or absence of *contraindications* in determining the question of operation.

The indications for operation are found (1) in the presence of cancer, (2) in the demonstration that it is not of long standing, and (3) (most important) the absence of signs of regional and remote metastasis. The recognition of cancer has already been discussed under diagnosis. The determination of the period of the disease is difficult, often impossible, revealed sometimes by the date of beginning pain, rarely by the size of the prostate, more accurately by the presence of metastases, the symptoms of which form the chief factors contraindicating operation.

Contraindications.—Under this heading will not be considered the rules governing operation in general, but only those signs which bear witness of secondary malignant complications by reason of which radical operation is obviously prohibited. These, as shown in the symptomatology, include the manifestations of carcinosis of the skeleton, of the glands, of the seminal vesicles, rectum, bladder, and pelvis.

The question of operation, because of the difficulty of diagnosis not only of the primary but metastatic disease, must often be made (even under improved clinical methods) problematic, so much so that the contention must be raised, Is it possible in any case to be sufficiently positive of early and uncomplicated prostatic carcinoma to justify operation? Answer to this question must await future clinical experience. One impressive example in the affirmative is given in Greene's case (see appendix). For the present, opinion must differ;

on one hand scepticism, the result of current prejudice against operation born of past failures; on the other, an optimism, sanctioned by pathological study and encouraging clinical results.

Our attitude should be broadened by a study of the position of surgery in malignant disease.

History is replete with instances of the shortcomings of surgery and of unwise conservatism, which have been responsible for a goodly share of the failures and the discouraging statistics. Under the guise of conservatism, there has been, and probably will be, that hesitancy, in the face of suspected and even certain malignant disease, which vacillates in order to make sure of the diagnosis and avoid error by observing its growth, and that tendency to doubt and to wait until action is the only thing left to do. Conservatism in the treatment of malignant disease, as conservative surgeons have constantly declared, is to be found in early and complete excision. It even goes farther than this, as exemplified in the recent plea of Dr. Maurice H. Richardson²⁷ under the formula, "Neoplasms, wherever situated, should, if possible, be removed, whatever their apparent nature." Such wise radicalism can alone limit the extent and mutilation of operative procedures and better their results.

Operative procedures have undergone retrograde modification from extensive pelvic ablation to intracapsular prostatectomy. Socin resected the coccyx and divided the anterior and posterior wall of the rectum. Rydygier used a long incision at the border of the sacrum, and Küster devised a combined suprapubic and perineal operation for removal of the bladder and prostate *en masse*. Zuckerkandl and Dittel recommended exposure of the prostate and seminal vesicles by a wide perineal incision. The results of operations undertaken in the past upon cases of obvious extensive growth have rendered all methods obsolete, so that no particular fashion of procedure is now recognized. The few who venture a word dismiss the subject of radical operation with the statement that removal is by prostatectomy as done for hypertrophy. The French

school have adopted the extra-capsular method of Proust and the more popular subcapsular method of Albarran. While enucleation of the prostate in a general way suffices to fill operative requirements, because operation is only admissible when the disease is supposedly limited to the prostate, to apply such procedure thus blindly and empirically is irrational on account of the impossibility of being sure of the exact extent of the disease. For this reason, procedure should first of all be exploratory, designed to permit of operative diagnosis before removal is attempted, in order to decide with more accuracy the actual degree of local involvement, the feasibility of continuing, together with probable prognosis. To this end the prostate may be thoroughly exposed by one of the various transverse perineal incisions and the bladder opened above. Upon exploratory findings must procedure be guided. From past experience, it would be folly in the presence of vesical or pelvic invasion to remove the prostate, except as a palliative measure for the relief of severe pain or urinary obstruction. If, however, extraprostatic disease is not manifest, prostatectomy should be proceeded with, though not, perhaps, by the usual methods, because here, again, conditions vary—altering operative requirements. Pathological anatomy teaches us that carcinoma may be situated in a portion of one lobe or more or less scattered throughout the recto-urethral portion of the prostate. Theoretically, then, when the first condition exists, partial prostatectomy, enucleation of one lobe, is sufficient; when the second obtains, the usual prostatectomy (either suprapubic or perineal) with removal of the retro-urethral or surgical prostate is enough; when urethral invasion is present, excision of the entire gland with the prostatic urethra is demanded. A discussion of the methods of carrying out these various degrees of prostatectomy is out of place here, except for a word in regard to total enucleation. This has been very easily (more so than in partial prostatectomies) and successfully accomplished by dividing transversely the membranous urethra and, as in all prostatectomies, intracapsular enucleation, which by said urethrotomy is greatly facilitated. The membranous

urethra below may be approximated with the vesical outlet. Before the wound is closed, digital examination of the seminal vesicles and pelvis should be made, merely to satisfy the mind of the operator concerning the possibility of their involvement.

While the method of operative procedure best suited to early carcinoma of the prostate must be evolved by future work, total enucleation (urethroprostectomy) would seem most appropriate because less difficult, and in view of the nature of the disease most complete. Certainly, methods of prostatectomy which deny sufficient exposure for thorough exploration are blind and unfit in prostatic cancer. Regarding urethroprostectomy, it is interesting to learn that Mr. Moynihan,²⁴ of Leeds, has recently reported a brilliant series of cases carried out by the suprapubic route for obstructive hypertrophy.

Palliative surgical measures have been recommended with due caution (1) in the form of prostatectomy, as a means of prolonging life and as a measure of last resort for the relief of pain, and (2) for the relief of urinary obstruction and infection. Removal of the prostate for the purpose of delaying the inevitable has been vociferously condemned despite the fact that Billroth, Czerny, and others have shown a lengthening of life from one to two years. Most recent observations refer to this practice as questionable except in rare cases.

Prostatectomy for the relief of pain is justifiable in those few cases in which pain is severe and medical relief ineffectual. Harrison mentions such a case (see appendix), the patient beseeching operation, which was followed by relief to the sufferer.

Urinary obstruction sometimes requires surgical intervention in the form of suprapubic cystotomy for permanent drainage. Rarely is perineal drainage used because of the interposition of the diseased prostate.

Röntgen-ray therapy has not as yet proved its usefulness in deep-seated tumors. Although untried in prostatic carcinoma, its value is doubtful, more particularly because this gland is enclosed within the bony pelvis, though this disadvantage may

be obviated by treatment from below. Harrison hesitatingly urges its use as a possible curative or palliative measure, and has placed it on trial in several cases. Unable so far to draw any conclusions, he has observed relief of pain with no ill effects. This treatment is worthy of a fair trial, for the prostate is not so deeply placed perineum.

Symptomatic treatment is directed to controlling the pain and urinary complications when they are present. For the former, opium in suppositories may be used as well as in other forms.

The treatment of urinary complications requires careful consideration in that the trauma of instrumentation may lead to destructive ulceration of the urethral and vesical mucosa. Instrumentation should be avoided in cancer of the prostate, especially when advanced. Fortunately, it is rarely necessary. Catheterism is to be delayed and shunned if possible. For cystitis and continued haematuria, irrigation by hydraulic pressure will usually suffice. In the event of failure to wash the bladder by hydraulic lavage or by soft catheter, rather than resort to the constant use of a rigid catheter, it may, perhaps, be best to establish permanent suprapubic drainage. For cystitis, the internal remedies have their restricted usefulness, and systematic lavage of the bladder is indicated according to the degree of infection. In ulcerative and gangrenous cystitis, more effective drainage is necessary. For haematuria, adrenalin works benefit.

Summary.—After scrutinizing closely and in more or less detail the subject of primary carcinoma of the prostate from different view-points, the picture exhibited may be thus briefly described. Occurring in the latter third of life, and in the normal, hypertrophied, or atrophic gland, prostatic cancer is characterized by restricted local growth; by deposits in the urethra, vesical trigone, seminal vesicles, and pelvic lymph-glands; and by diffuse metastasis in the marrow of the bones of the trunk in the form of osteolytic and osteoplastic carcinosis. Symptomatic of the prostatic tumor are pain, tender and hard nodosity of the gland, and in hypertrophy-cancer the

phenomena of urinary obstruction. Signs of metastases are found in certain urinary symptoms, as haematuria from ulceration of the prostatic urethra, in enlarged pelvic and inguinal glands, and in pain, tenderness, and small tumors of the bones with myelocytosis and qualitative alteration in the erythrocytes. Of the diseases with which confusion is possible are senile enlargement, stone, cyst, neuroses, and inflammation of the prostate; also cancer of the rectum and bladder, vesical stone, etc. The prognosis, invariably most grave when untreated, from an anatomic stand-point and from recent operative experience, is better than in many malignant diseases with radical surgical treatment.

The treatment of carcinoma is, in early cases, by radical surgical intervention; in cases with vesical, glandular, and osseous metastases, strictly palliative and symptomatic. Radical operation consists in prostatectomy and, because of the nature of the disease, a urethroprostectomy, preferably by the combined suprapubic and perineal method, so designed that exploration for an accurate operative diagnosis may precede enucleation.

In Conclusion.—It has been the object of this paper to assemble all the available facts and creditable theories concerning carcinoma of the prostate. This has been attempted because (as previously stated) many of the modern books are in traditional error; because during the past few years definition has been given to an indefinite pathology; and because at this time, when much is being written about prostatic hypertrophy, little notice has been taken of cancer.

A study of carcinoma prostatæ leads to many conclusions, of which the following may be premised:

1. That this disease is sufficiently common and so frequently unrecognized—mistaken for simple enlargement—as to actuate more intelligent and accurate clinical observation upon all elderly men. Exclusion of cancer and watchfulness of its development in all cases of hypertrophy are indicated. The doctrine that "Prostatic hypertrophy is at all times easy of diagnosis" should be modified.

2. That cancer of the prostate is most distinctly operable before metastasis has taken place to regional or remote organs, and as distinctly inoperable after secondary vesical, glandular, and skeletal invasion. That the high percentage of operative cures reported from the French clinics presages a promising future.
3. That radical operation should prescribe liberal perineal exposure of the prostate with preliminary exploration of the bladder and periprostatic structures, and total intracapsular enucleation—urethroprostectomy. Prostatectomy *per se* is procrustean.
4. That there is opportunity for further pathological investigation,—particularly the careful post-mortem examination of all senile prostates,—for systematic clinical observation, and for operative improvement. It will be interesting to become better acquainted with the actual frequency of prostatic cancer, with the possibilities of early diagnosis, with the osseous phenomena and blood changes, and with the possibilities of surgery as a radical curative measure.

APPENDIX.

The following cases in abstract are appended in order to illustrate as comprehensively as possible the various points in the foregoing text. These particular ones are chosen because collectively they bring out both the common and bizarre phenomena, and because the data in each are quite replete.

1. CASE by SIDNEY M. CONE from the clinic of Dr. W. S. Halsted.—Aged seventy-five years; white. Entered hospital complaining of painful swelling over right tibia and symptoms of cystitis for which he had been treated and discharged improved a year previous. "Notes made at this time by Dr. Young refer to the great enlargement of the prostate and probable existence of a tumor. Careful examination excluded the existence of a tumor of other organs." Amputation by Dr. Halsted was followed by uneventful recovery and dismissal of patient to home. The operative diagnosis was held to be that of carcinoma rather than sarcoma, and so proved by the microscope. Six months later patient had lost thirty pounds, was much emaciated, but cystitis much improved. Death seven months after operation.

Autopsy.—Prostate much enlarged, measuring six by five by five centimetres. Lateral lobes symmetrically enlarged. Middle lobe enlarged. Nothing distinctive on cut surface.

Regional Metastasis.—Backward from the lateral, particularly the middle lobe, is a mass spreading into the seminal vesicles; absence of urethral and bladder invasion; "prostatis and haemorrhoidal veins plugged with phleboliths."

Remote metastasis was found in the bones, namely, lumbar vertebrae, second rib, ilium; osteoplastic carcinosis of tibia (amputated), second rib and ilium. Glandular metastasis was noticeably absent, except in one bronchial gland. No internal metastases.

In microscopic appearance, the tumor in the prostate, bones, and bronchial lymph-gland was sufficiently similar to conform to one description in which two appearances were presented, "first, a tubular adenomatous growth, cystic in places; second, a conglomerate mass of cells which have lost their arrangement in tubules," resembling round-cell infiltration.

2. CASE by R. H. GREENE.—Aged fifty-nine years. Gonorrhœa forty years previous. No urinary disturbance since, except slight burning at micturition during past few months. After indulging freely in champagne, retention developed, relieved by catheterization. Function returned. From this time on suffered pain in region of prostate and rectum. Seen by Dr. Greene three months later.

Examination.—Well-nourished man, residual urine small, urine negative, apparently no third lobe enlargement, right lobe slightly enlarged by urethral examination (rectal examination negative). Treated by tonics, sedatives, and irrigations without effect. Patient complained of pretty constant pain and much depressed by it, so that operative interference for its relief became imperative. Diagnosis at the time, probable encapsulated abscess or stone of the prostate. Operation (prostatectomy by the Alexander method) was successful, though convalescence delayed on account of a small recto-urethral fistula. Pathological report by Dr. Harlow Brooks: In the left lobe, moderate connective-tissue hyperplasia and small areas of round-cell infiltration; in the right lobe "a nodule of more compact structure than the surrounding tissue and measuring about five centimetres in diameter." "The nodule of compact tissue is made up of islands of proliferating epithelial cells. This growth is adenocarcinoma." Apparently it has been of rather recent formation.

3. CASE by REGINALD HARRISON.—Professional man, aged sixty-one years. Complained of frequency of micturition. No residual urine. Prostate by rectal examination was found to be large and hard. "It was noted, however, that the rectum was freely movable over it, and that the growth was not unduly fixed within the pelvis." Patient was not seen until nine months later, when mictural frequency had so increased, and with it the necessity for catheterization, that operation was urgent and suprapubic prostatectomy performed. What was apparently a fibro-adenoma was enucleated with some difficulty. Evidence of bladder distention found and ureteral orifices were patent to the finger. Gross appearance of the tumor was that of adenoma, which the first microscopic examination supported. A further examination unmistakably indicated its carcinomatous nature. Three months after operation patient was in excellent health and passing

urine quite naturally. One month later had slight attack of haematuria. One year later the abdominal cicatrix and contiguous glands had largely become involved in carcinoma, with oedema of legs and scrotum.

4. CASE by REGINALD HARRISON.—Patient, aged sixty-four years, complained of frequency of micturition with occasional dribbling. Catheter had previously been passed,—no residual urine. History of former renal colic with passage of gravel. "Examination by rectum showed the prostate to be extremely hard, particularly at one point, where it had the sensation as if a stone was impacted there." Patient complained of dull aching about the buttocks and thighs. "He was losing flesh." Later increase in size and hardness of the prostate necessitated catheterism. "Occasionally a few drops of blood were passed." No enlarged glands in loins or femoral regions detected. Patient urged operation for pain. "I gave it as my opinion that the case was an unfavorable one for prostatectomy, as it was not unlikely the growth would recur, and there was no guarantee that the whole of the disease could be removed." It could not be denied that the growth might not be of one of those densely fibrous prostates, though the weight of evidence was against this. However, at patient's request, operation (suprapubic prostatectomy) was performed. Prostatic mass could not be enucleated entire, but was removed in portions. Patient received immediate relief, but progress was disappointing. Recurrence and death followed in four months. "Secondary growth manifested itself in the spine about the ninth and tenth dorsal vertebrae." Microscopical examination of prostate: "The periphery of the mass was adenomatous, whilst the centre was carcinomatous." The growth cut like scirrhus of the breast and yielded cancer juice.

5. CASE by EDUARD KAUFMANN.—Aged seventy-three years. Duration of illness, several months. Symptoms: Pain in back and abdomen; tenderness on pressure over lower portion of the crest and over the spinous processes of the lumbar vertebrae. Absence of vesical or rectal symptoms; increasing debility. Post-mortem examination of prostate; Both lobes slightly enlarged and irregularly nodose; the left about the size of a pigeon's egg and very hard, with smooth, grayish cut surface, dotted with white spots; the right lobe smaller, nodular, hard, with only one yellowish-white spot of the size of a pea upon the gray cut surface. Microscopical diagnosis: Adeno carcinoma with transition into carcinoma solidum. Complicating diseases: Hypertrophy and dilatation of the heart; double-sided hydrothorax, emphysema, and bronchitis. Metastases of neighboring organs: Small nodes in the bladder and pinhead nodules in the rectovesical pouch. Metastases in the glands: Pelvic, retroperitoneal (as far as kidneys and spleen), mesenteric, inguinal (pea-size) and left supraclavicular (walnut-size). In the right femur (upper fourth) distinct cancer islands of size of hazel-nut. (In the ribs and lumbar vertebrae numerous fibrocartilaginous exostoses, non-cancerous.)

6. CASE by EDUARD KAUFMANN.—Aged sixty-seven years. Duration of disease, nine months. Symptoms: Pain in right thigh in region of sciatic nerve; rapid loss of strength. Clinical diagnosis: Chronic rheumatism. Examination of prostate at autopsy: very hard, both lateral

lobes as large as a hen's egg, yellowish-white cut surface, porous in places. Middle lobe prominent, with two projections into the vesical trigone, and tubercled appearance of mucous membrane and of prostatic urethra. Microscopic diagnosis: Carcinoma solidum with cubical character of cells. In part exquisite infiltration with penetration into the blood-vessels. Regional metastases: In the bladder and urethra (fine nodules), in the seminal vesicles and vasa deferentia. Remote metastases: Lumbar vertebrae, ribs, femur, humerus, clavicles, and skull (osteoplastic); glands around the aorta at the level of the kidneys; left kidney and adrenal, liver and pleura.

7. CASE by EDUARD KAUFMANN.—Aged forty-eight years. Duration, eighteen months. Symptoms: Pain in sacrum, in both knees, headache, and vertigo; liver enlarged to four fingers'-breadth below costal margin, hard, granular, and tender; left hip tender to pressure; gait paretic; plantar and patellar reflexes abolished; increasing weakness. Clinical diagnosis: Carcinoma of lumbar vertebra (?), of liver, and spleen. Post-mortem examination of prostate: Right lobe as large as a plum, with soft, white nodes; left lobe similar. Complicating lesions: Haemorrhagic pleuritis (left), pachymeningitis haemorrhagica, emphysema, and bronchitis. Metastases: Lumbar vertebrae, femur, ribs, pelvis, and humerus (osteoplastic); retroperitoneal, mesenteric, bronchial, and mediastinal (size of fist) lymph-glands; liver, lungs, pleura, and kidneys.

8. CASE by EDUARD KAUFMANN.—Aged seventy-two years. Duration, several months. Symptoms: Rheumatoid pains in sacrum and thighs; diffuse intrapelvic pain; frequency of micturition with cloudy urine and catheter-life; hard tumor of uncertain contour over crest of ilium (left); skiagraph negative; increasing loss of flesh; later, nodes in pelvis and fracture of clavicle. Clinical diagnosis: Carcinoma of the prostate, rectum, and the bones. Prostate at autopsy: The size of one's fist and hard; right lobe completely carcinomatous; in left sonic prostatic tissue remaining. Microscopic diagnosis: Carcinoma simplex, solidum. Local metastases: Invasion of neck of bladder; mouth of right ureter surrounded by ulcerated tumor mass; nodes in corpus spongiosum, corpora cavernosa, and sileus coronarius, of penis, seminal vesicles, rectum, and rectovesical pouch infiltrated with nodules; general invasion of pelvic veins. Distant metastases: Iliac, sacral, and periaortic glands (small and hard), left inguinal markedly enlarged; os ischii (tumor as large as child's head), left scapula and clavicle (fractured), one rib (fractured), left tibia and fibula, and calvarium (in part osteoplastic); pancreas and dura mater cerebralis.

9. CASE by EDUARD KAUFMANN.—Aged fifty-eight years. Duration of illness, one year. Symptoms: Pain in sacrum. Prostate post-mortem: Left lobe somewhat hard and slightly enlarged, with isolated nodules projecting from the cut surface; right lobe rather soft with one very hard, extremely prominent node. Complicating lesions: Apoplexis vetus and a cloudy and fibrous degeneration of the myocardium. Metastases: Pelvic glands (size of nuts); vertebrae, pelvis, ribs, and sternum (osteoplastic).

10. CASE by EMIL BUREKHARDT.—Aged seventy years. Several years previous perineal prostatectomy had been done and a year and a half later castration. Two years after last operation paraplegia set in, preceded by lancinating pains and spastic contractions in both legs. Death occurred four weeks later from pneumonia. Autopsy: A cancer node in right lobe of prostate (size of a filbert), a pea-sized node in left lobe. A markedly protruding middle lobe as large as a pigeon's egg, totally carcinomatous. Both seminal vesicles invaded. Skeletal metastasis: Vertebrae, left ilium, right femur, sternum, and right humerus. Glands: Pelvie, retroperitoneal, and inguinal. Also pleura and spinal dura mater. In the latter, a node as large as a cherry at the level of the first lumbar vertebra, with degeneration of the cord at this point and cancerous invasion of the first right lumbar nerve.

LITERATURE.

- ¹ Albaran, J., and Hallé, N. Hypertrophie et néoplasies épithéliales de la prostate. *Annales des maladies des organes génito-urinaires*, February and March, 1900.
- ² Belfield, W. T. Diseases of the Prostate. *Morrow's System of Genito-Urinary Diseases, Syphilology, and Dermatology*, Vol. i, 1893.
- ³ Belfield, W. T. Progressive Medicine, December, 1900.
- ⁴ Belfield, W. T. Progressive Medicine, December, 1903.
- ⁵ Braun, L. Ueber osteoplastisches Carcinom der Prostata, zugleich ein Beitrag zur Genese der perniciösen Anämie. *Wiener medicinische Wochenschrift*, 1896, Nos. 13 and 14.
- ⁶ Burekhhardt, Emil. Die malignen Neubildungen der Prostata. *Socin and Burekhhardt's Die Verletzungen und Krankheiten der Prostata*, Stuttgart, 1902.
- ⁷ Cicelanowski, S. Ueber die sogenannte Hypertrophie der Vorsteherdrüse und über anatomischen Grundlager der senilen Insuffizienz der Blase. *Centralblatt für Chirurgie*, 1896, No. 32.
- ⁸ Cone, S. M. A Case of Carcinoma Metastasis in Bone from a Primary Tumor of the Prostate. *Bulletin of the Johns Hopkins Hospital*, May, 1898, Vol. ix.
- ⁹ Grandon, L. R. G. The Pathogenesis and Pathological Anatomy of the Enlarged Prostate. From the pathological laboratory of the Boston City Hospital, *ANNALS OF SURGERY*, December, 1902.
- ¹⁰ Engellbach, P. Les tumeurs malignes de la prostate. *Thèse de Paris*, 1888.
- ¹¹ Fenwick, E. Harry. Primary Malignant Disease of the Prostate Gland. *Edinburgh Medical Journal*, 1899, p. 16.
- ¹² von Frisch, Anton. Die Krankheiten der Prostata. Wien, 1898.
- ¹³ von Frisch, Anton. Klinische Untersuchungsmethoden. *Frisch and Znckerkandl's Handbuch der Urologie*, Vol. iv.
- ¹⁴ Greene, R. H., and Brooks, H. The Nature of Prostatic Hypertrophy. *The Journal of the American Medical Association*, April, 26, 1902.
- ¹⁵ Greene, R. H. Cancer of the Prostate. *New York Medical Journal*, October 24, 1903.

¹⁴ Guépin, A. Cancer de la prostate. *Presse médicale*, 1896.

¹⁵ Harrison, Reginald. Remarks on Cancer of the Prostate and the Selection of Cases for Suprapubic Prostatectomy. *The British Medical Journal*, July 4, 1903.

¹⁶ Julien, Louis. Contribution à l'étude clinique du cancer de la prostate. *Thèse de Paris*, 1895.

¹⁷ Kaufmann, Eduard. Pathologische Anatomie. *Soem and Burkhardt's Die Verletzungen und Krankheiten der Prostata*, 1902.

¹⁸ Kaufmann, Eduard. *Lehrbuch der Speziellen Pathologischen Anatomie*. Berlin, 1901.

¹⁹ Keyes, E. L., and E. L., Jr. The Surgical Diseases of the Genito-Urinary Organs, 1903.

²⁰ Kurpinweit, O. Zur Diagnose von Knochenmarksmetastasen bei malignen Tumoren aus dem Blutbefunde. From the clinic of Professor Liebtheim, Königsberg, *Archiv für klinische Medizin*, September, 1903, Band lxxii, Hefte 5 and 6.

²¹ Labadie, G. Du cancer de la prostate. *Thèse de Lyon*, 1905.

²² Moynihan, B. G. A. On Removal after Suprapubic Cystotomy of the Prostate and Prostatic Urethra for Senile Enlargement of the Prostate. *ANNALS OF SURGERY*, January, 1904.

²³ Oraison, H. Du cancer primitif et limité de la prostate et de son traitement par le prostatectomie périneale. *Annales des maladies des organes génito-urinaires*, May, 1903.

²⁴ von Recklinghausen, F. Die fibröse und deformirende Ostitis der Osteomalacie und die osteoplastischen Carcinome in ihren gegenseitigen Beziehungen. *Festschrift zu Virchow's 71. Geburtstag*, Berlin, 1891.

²⁵ Richardson, Maurice H. Neoplasms, wherever situated, should, if possible, be removed, whatever their Apparent Nature. Report of the Southern Surgical and Gynaecological Association, *The Journal of the American Medical Association*, January 9, 1904.

²⁶ Sasse, F. Ostitis carcinomatosa bei carcinom der Prostata. *Archiv für klinische Chirurgie*, 1894, Band xlvi, S. 596.

²⁷ Thompson, Sir Henry. Carcinomatous Deposits in the Prostate Gland. *Pathological Transactions*, London, 1854.

²⁸ Weber, F. Parkes. Multiple Myeloma (Myelomatosis) with Bence-Jones Proteid in the Urine. *The American Journal of the Medical Sciences*, October, 1903.

²⁹ Wolff, Richard. Ueber die bösartigen Geschwülste der Prostata insbesondere über die Carcinome derselben. *Deutsche Zeitschrift für Chirurgie*, July, 1899, Band lii, Hefte 3 and 4.